Determination of Intended Use for 510(k) Devices – Guidance for Industry and CDRH Staff

This document is intended to provide guidance. It represents the Agency's current thinking on the above. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

Prepared by
Office of Device Evaluation
Center for Devices and Radiological Health

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Until May 26, 1998, comments and suggestions regarding this document should be submitted to Docket No. 98D-0081, Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 12420 Parklawn Drive (HFA-305), Room 1-23, Rockville, MD 20857. Such comments will be considered when determining whether to amend the current guidance.

After May 26, 1998, comments and suggestions may be submitted at any time for Agency consideration to Heather Rosecrans, Chief, Premarket Notification Section, HFZ-404, Office of Device Evaluation, 9200 Corporate Boulevard, Rockville, Maryland. Comments may not be acted upon by the Agency until the document is next revised or updated. For questions regarding the use or interpretation of this guidance contact Heather Rosecrans at (301) 594-1190.

Additional Copies: World Wide Web/CDRH home page at http://www.fda.gov/cdrh or CDRH Facts on Demand at 1-800-899-0381 or 301-827-0111, specify number 857 when prompted for the document shelf number.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
Center for Devices and Radiological Health
Rockville, MD 20850

Purpose

The purpose of this guidance[1] is to establish standard operating procedures to be followed by Office of Device Evaluation (ODE) review staff in carrying out Section 513(i)(1)(E) of the Federal Food, Drug, and Cosmetic Act (the Act) as amended by Section 205 of the FDA Modernization Act of 1997.

Background

As stipulated in Section 513(i) of the Act, FDA may issue an order of substantial equivalence only upon making the determination that the device to be introduced into commercial distribution has the same intended use as the predicate device and is as safe and effective as a legally marketed device. New Section 513(i)(1)(E) of the Act limits the determination of the intended use of a device that is the subject of a premarket notification (510(k)) to the proposed labeling contained in the submission.

"Labeling" is defined in Section 201(m) of the Act as "all labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article." Proposed labels, labeling, and advertisements sufficient to describe the device, its intended use, and the directions for use are required to be submitted in a 510(k) for review during the substantial equivalence determination. (See 21 CFR 807.87(e))

Thus, based on the above, the intended use of a device shall be determined by an evaluation of the proposed labeling for the device as submitted in the 510(k). While this is a new statutory requirement, it is important to note that it is not different from the manner in which 510(k)s have traditionally been reviewed. As stated in ODE Blue Book Memorandum #K86-3 entitled,

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"Guidance on the Center for Devices and Radiological Health's Premarket Notification Review Program (June 30, 1986)," "Ordinarily, intended use is determined by reference to 'labeling' or promotional claims; only in rare cases might it be necessary to infer intended use from other types of information."

In addition to the restrictions regarding the determination of intended use, the new law defines the procedures to be followed if the Director of the Office of Device Evaluation (ODE) believes "that there is a reasonable likelihood that the device will be used for an intended use not identified in the proposed labeling for the device" and "that such use could cause harm." (See Section 513(i)(1)(E)(ii)). Below, the procedures to be used by ODE staff and the Office Director in complying with the new statute are described.

Procedures

A. Procedures for Division Staff

In determining the intended use of a device that is the subject of a 510(k), reviewers should continue to follow Blue Book #K86-3 guidance which states that the intended use of the device should be determined by the proposed labeling for the product. As defined above, this includes the actual label for the device and any accompanying information such as directions for use and promotional materials. Claims may also be important in determining the intended use of the device. ODE is currently developing a guidance document entitled, "Claims and 510(k) Submissions -- Guidance for Reviewers and the Regulated Industry," which will help to address the impact claims may have on the determination of the intended use of a device.

In reviewing the premarket notification, there may be rare instances in which the design of the device or published literature referencing the subject device or a similar device, would lead one to believe that there may be an intended use different than that appearing in the labeling. If this situation occurs, the reviewer should bring the discrepancy to the attention of senior division management.

The reviewer and division management should consider:

(1) Whether there is a <u>reasonable likelihood</u> that the device will be used for an intended use not identified in the proposed labeling for the device, **and**

(2) If such use <u>could cause harm</u> to the patient or the consumer.

If, while reviewing the 510(k), the division makes the determination that there is a reasonable likelihood that the device will be used for an intended use other than that in the proposed labeling (hereinafter referred to as off-label use) that could cause harm, the review of the submission should proceed as follows. All deficiencies with regard to the submission, except those regarding

the off-label use, should be discussed with the firm and resolved in accordance with established division procedures. Once all other outstanding issues have been resolved, the concern about the off-label use should be promptly brought to the attention of the Chief of the Premarket Notification Section (Chief), Program Operations Staff (POS). The Chief will be responsible for coordinating the resolution of the off-label use issue with the Office Director. If, while reviewing the 510(k), the reviewer observes no deficiencies that prevent a substantial equivalence recommendation other than the concern regarding an off-label use, the division should bring that concern to POS as soon as the review of the 510(k) is complete.

B. Procedures for the Office Director

When the Office Director receives a referral from POS regarding off-label use, the Director will evaluate the information provided and determine if the two statutory criteria are met. That is, the Office Director must decide if there is a reasonable likelihood that the device will be used for an intended use not identified in the proposed labeling **and** if such use could cause harm to the user.[2] If the Office Director determines that these criteria are not met, this finding should be documented and the device should be promptly found substantially equivalent (SE). If, however, the Office Director believes that the two criteria are met, the 510(k) submitter must be provided an opportunity for consultation in the most efficient manner possible.

1. Consultation

   Consultation between the Office Director and the 510(k) submitter may take the form of a telephone call or a meeting. The form of the consultation will be determined by whichever method best satisfies the needs of both parties and offers the most expedient path to resolution.

2. Resolution

   Following consultation, one of three actions may ensue. First, after discussing the off-label use issue with the firm, the Office Director may decide that the two criteria regarding off-label use have not been met and direct the division to issue a substantial equivalence determination. Alternatively, if the Office Director believes that there is a reasonable likelihood that the device will be used for an intended use not identified in the proposed labeling and that this use could cause harm, the firm will be provided an opportunity to: 1) modify the device design to address the off-label use **or** 2) request a written determination from the Director. If the modified design adequately satisfies the Agency's concerns regarding the off-label use, a routine substantially equivalent determination can be

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[2] For purposes of this document, the term "user" may be the patient, health care provider, or any other person who has the device used on or in him/herself or who uses the device him/herself.

rendered. Finally, if the firm either fails to modify the device such that the off-label use issue is resolved or decides to request a written determination from the Director, the Office Director must issue an "SE letter with Limitations" within 10 days of the consultation.

The "SE letter with Limitations" ("the letter") will advise the 510(k) submitter that the Office Director has determined: (1) that there is a reasonable likelihood that the device will be used for an intended use not identified in the proposed labeling for the device and (2) that such use could cause harm. The letter must also specify appropriate limitations regarding the off-label use to be included in the labeling for the device. These labeling limitations may be expressed using the standardized language provided in the boilerplate letter (Attachment 1) or may include other labeling limitations specific to the device and the off-label use, as determined by the Office Director. The letter will require these limitations to be added to the Precautions, Warnings, Contraindications, or other appropriate section of the device's labeling. Finally, the letter must stipulate that the device is only substantially equivalent if the labeling for the device conforms to the limitations specified in the letter. The boilerplate "SE letter with Limitations," which was drafted for use under the conditions described above, can be found on the H drive under "K-32."

Special Notes

1. As stipulated in Section 205 of the FDA Modernization Act, the Office Director may not delegate any of the responsibilities specified in this memorandum.

2. According to ODE Blue Book #K97-1 entitled, "Deciding When to Submit a 510(k) for a Change to an Existing Device," manufacturers are permitted to make certain labeling changes without submission of a new 510(k). The labeling limitations included in the "SE letter with Limitations," however, are required by Section 513(i)(1)(E) of the Act. Therefore, a new 510(k) <u>is</u> required before these limitations are modified in any way or removed from the device's labeling.

3. This provision will have no legal effect after expiration of the five-year period beginning on November 21, 1997, the enactment date of the Food and Drug Administration Modernization Act of 1997.

Effective Date

This memorandum is effective on February 19, 1998, the effective date of Section 205 of the FDA Modernization Act.

Philip J. Phillips
Deputy Director for Science and
Regulatory Policy

Attachment

K-32
SUBSTANTIALLY EQUIVALENT LETTER WITH LIMITATIONS
[510(k) HOLDER -- COMPANY NAME]
[C/O COMPANY REPRESENTATIVE, THIRD PARTY, OR CONSULTANT, (IF ANY)]
[COMPANY REPRESENTATIVE, THIRD PARTY, OR CONSULTANT ADDRESS]
[CITY, STATE, ZIP CODE]

Re: [510(k) NUMBER]
Trade Name: [ ]
Regulatory Class:
Product Code: [ ]
Dated:
Received:

Dear [ADDRESSEE]:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act). You may, therefore, market the device, subject to the general controls provisions of the Act and the limitations described below. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

The Office of Device Evaluation has determined that there is a reasonable likelihood that this device will be used for an intended use not identified in the proposed labeling and that such use could cause harm. Therefore, in accordance with Section 513(i)(1)(E) of the Act, the following limitation must appear in the [**OPTION**: Precautions/Warnings/Contraindications] section of the device's labeling:

[OPTION: CHOOSE ONE OF THE FOLLOWING FOUR OPTIONS]

1. The safety and effectiveness of this device for use in the treatment of [insert disease or condition] has not been established.

2. The safety and effectiveness of this device for use in the diagnosis of [insert disease or condition] has not been established.

3. The safety and effectiveness of this device for use in the performance of the [insert procedure] has not been established.

4. Other (As determined by the Office Director).

[END OF OPTION]

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and permits your device to proceed to the market. This letter will allow you to begin marketing your device as described in your 510(k) premarket notification if the limitation statement above is added to your labeling, as described.

Please note that the above labeling limitations are required by Section 513(i)(1)(E) of the Act. Therefore, a new 510(k) is required before these limitations are modified in any way or removed from the device's labeling**.**

If you desire specific information about the application of other labeling requirements to your device (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-__. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Susan Alpert, Ph.D., M.D.
Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure